SHORT CUTS

WHAT'S NEW IN THE OTHER GENERAL JOURNALS

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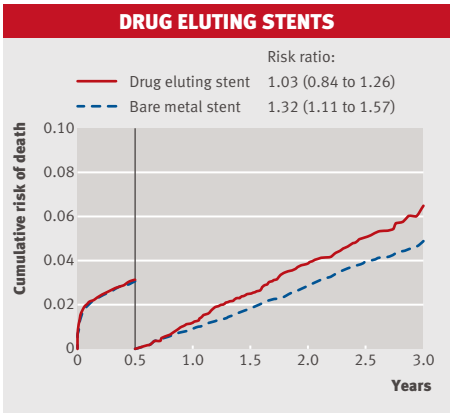
Drug eluting stents may increase long term mortality due to late stent thrombosis



Compared with bare metal stents, drug eluting stents seem to have an increased risk of late stent thrombosis, a potentially fatal complication of percutaneous coronary revascularisation. A recent cluster of five research papers and several commentaries shows the complexities of ascertaining which type of stent is better in the long run. The definitive evidence is still a long way off.

There seems to be no doubt that, in the short term, drug eluting stents reduce the need for revascularisation by about a half. In the longer term, however, increased risk of late stent thrombosis might translate into increased risk of death and non-fatal myocardial infarction.

Four recent trials (extensions of the original research that was the basis for getting drug eluting stents approved and which had less than 50% power to detect a doubling of the risk of death in patients for whom treatment with drug eluting stents is approved) failed to show a difference between groups for increased risk of death and non-fatal myocardial infarction. But a large, Swedish non-randomised study found that after six months the risk of death started to increase for people treated with drug eluting stents, compared with those with bare metal stents. At three years, the adjusted risk of death was 1.3-fold higher.

Drug eluting stents are approved only for clinically stable patients without serious comorbidities and with newly diagnosed coronary lesions up to 3 cm long. However, less than 60% of people treated with drug eluting stents today fit this profile. Off-label use in people with more serious disease is common.

Until definitive answers are available on the long term safety of drug eluting stents, it might make sense not to use them off-label, suggests one of the commentaries (http://content.nejm.org/cgi/content/full/NEJMp068304/DC1).

N Engl J Med 2007; 356:989-97; 998-1008; 1009-19; 1020-9; 1030-9

New models predict more accurately women's cardiovascular risk

Two new algorithms for predicting women's cardiovascular risk have been developed and validated in a cohort of nearly 25 000 women (derived from the women's health study), who were healthy at enrolment and prospectively followed up for a median of 10 years.

The algorithms, which take into account new risk factors as well as the traditional ones, were developed on the basis of recorded cardiovascular events in two thirds of the cohort. The researchers validated the algorithms by comparing predicted and observed outcomes in the remaining third of the cohort.

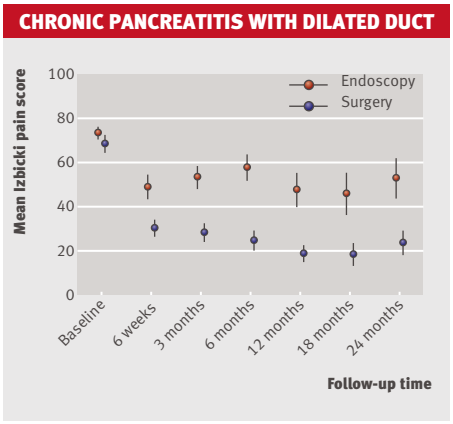
Compared with the currently used prediction scores based on the US Adult Treatment Panel (ATP) III guidelines, the new algorithms showed marked improvements: they reclassified 40% to 50% of women currently in the intermediate risk category to either a higher risk or a lower risk category, to more accurately predict the observed events.

Model B (the Reynolds risk score), which is somewhat less accurate but easier to use than the more extensive model A, takes into account age, systolic blood pressure, haemoglobin A_{1c} in women with diabetes, current smoking, total and high density lipoprotein cholesterol levels, high sensitivity C reactive protein, and parental history of myocardial infarction before age 60 years (www.reynoldsriskscore.org).

For women at low risk, neither of the new algorithms showed improvements over the ATP III score.

JAMA 2007;297:611-9

Surgery is better than endoscopy for chronic pancreatitis with dilated duct



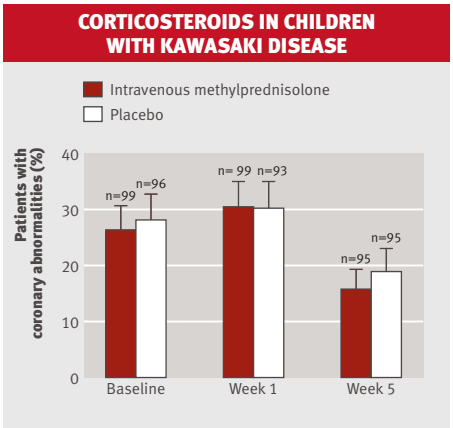
A trial randomised 39 people with symptomatic chronic pancreatitis and a distal obstruction of the pancreatic duct to endoscopic transampullary drainage of the pancreatic duct or operative pancreaticojejunostomy. Most patients had extensive disease with a combination of strictures and stones; people with an inflammatory mass were excluded from the study. The safety committee stopped recruitment early because an interim analysis clearly favoured surgery.

In the two years of follow-up, patients who received surgery had lower pain scores, better physical health, and fewer additional procedures than people who received endoscopy. Three quarters of patients who had surgery had complete or partial pain relief at the end of follow-up, compared with less than a third who had endoscopy. The groups had similar rates of complications, length of stay in hospital, and changes in pancreatic function.

The considerable difference in the pain scores between the groups (25 *v* 51) at the end of follow-up translates to clinical differences between having no pain and having pain daily, or between taking no sick leave for pain and being permanently unable to work, say the authors. Hope for

additional improvement comes from the fact that pancreaticojejunostomy may in the future become a less invasive laparoscopic procedure.
N Engl J Med 2007;356:676-84

Pulse corticosteroids don't help most children with Kawasaki disease



We know that treatment with aspirin and high doses of intravenous immunoglobulin improves outcomes for most children with Kawasaki disease—for example, reducing the occurrence of potentially fatal coronary artery aneurisms from 25% (seen in the natural course of the disease) to up to 5% with treatment. Adding corticosteroids early in the treatment doesn't seem to improve outcomes any further, although previous studies suggested that this strategy might be beneficial for children with this acute vasculitis of unknown cause.

A multicentre double blind trial randomised 199 children with Kawasaki disease to receive (before standard treatment) either 30 mg per kilogram of body weight of intravenous methylprednisolone in a single pulse dose or placebo. At five weeks, the groups had similar coronary dimensions as assessed by two dimensional echocardiography, length of stay in hospital, duration of fever, rates of repeated treatment with immunoglobulin, and rates of adverse events.

A subgroup analysis showed that children with persistent fever had better coronary outcomes with corticosteroids than without. Children at highest risk of resistance to standard treatment may therefore benefit from corticosteroids, but adding corticosteroids to standard treatment in children with Kawasaki disease does not seem to be justified.
N Engl J Med 2007;356:663-75

New antenatal blood test for Down's syndrome looks promising

Antenatal screening for Down's syndrome has come a long way since late amniocentesis was an older woman's only option. But the search continues for a simple blood test that can tell a woman in early pregnancy whether her baby has trisomy 21. Researchers are currently focusing on the fetal DNA found in maternal blood. One emerging technique uses single mutation polymorphisms to distinguish fetal DNA from maternal DNA, and researchers from the US recently used it to count the number of fetal chromosomes in blood samples from 60 women. Eight of the women were tested in the first trimester.

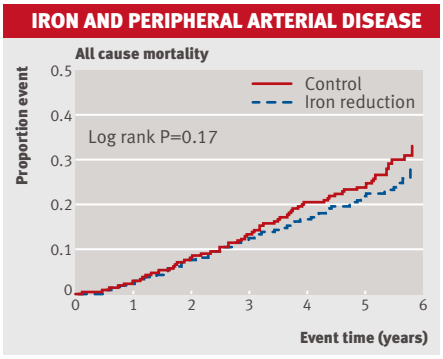
Three women had fetuses with trisomy 21. The new blood test picked up two of them, giving a sensitivity and a positive predictive value of 66.7%. A third woman had a false positive blood test result, and a fourth had a false negative one. The test's specificity and negative predictive value were both 98.2%. Overall, the test was about as accurate as current serum screening tests, although these results must be considered preliminary. We can be cautiously optimistic that this avenue of inquiry will eventually come up with an accurate and non-invasive test for Down's syndrome, says an accompanying editorial (pp 440-2). But we are not there yet.
Lancet 2007;369:474-81

How much fish should pregnant women eat?

We know that a pregnant woman's fish consumption is beneficial for her child's neurodevelopment, but we are not sure what amount optimally balances these benefits and the harms from trace contaminants. Women in the US are currently advised not to eat more than 340 g (three portions) of seafood each week, but a recent, large, UK cohort study from Bristol suggests that a somewhat higher intake might be better.

The study enrolled nearly 12 000 women and followed up their offspring at age 8 years. Compared with children of mothers who ate less seafood, children whose mothers ate more than three servings of seafood each week during pregnancy had better verbal IQ, more positive social interactions, and better fine motor, communication, and social development scores. The study was extensively adjusted for socioeconomic, dietary, and perinatal confounders.
Lancet 2007;369:578-85

Phlebotomy didn't improve outcomes in peripheral arterial disease



The hypothesis that excess iron contributes to cardiovascular disease (iron-heart hypothesis) was postulated in an attempt to explain why the risk of myocardial infarction in women after the menopause increases with age. The hypothesis incriminates excess body iron in the pathophysiology of cardiovascular plaques, through iron catalysed, free radical mediated, oxidative stress.

Much biochemical understanding supports the theory, but most observational studies have failed to show the association between biomarkers of body iron and risk of cardiovascular disease.

A recent trial (part of the US Department of Veterans Affairs Cooperative Studies Program) randomised 1277 people (99% of them men) with symptomatic but stable peripheral arterial disease to usual care or to the phlebotomy regimen designed to reduce iron stores but avoid iron deficiency. During the mean follow-up of four and a half years, the researchers found no difference between the studied groups in all cause mortality or the composite outcome of death, non-fatal myocardial infarction, or stroke.

However, the trial had only 68% power to detect a 30% reduction in mortality. The negative results therefore can't refute the iron-heart hypothesis. The accompanying editorial (pp 639-41) discusses groups of people, such as women after the menopause, in which it still might make sense to study interventions based on the hypothesis. But the author warns that we do have interventions that we know work for preventing atherosclerosis: exercise and weight control.
JAMA 2007;297:603-10